SYSTEMATIC REVIEW OF CLINICAL DECISION SUPPORT INTERVENTIONS WITH POTENTIAL FOR INPATIENT COST REDUCTION

by

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STATEMENT OF THESIS APPROVAL

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ABSTRACT

The purpose of this thesis was to systematically review trials of clinical decision support interventions with the potential to reduce inpatient costs, so as to identify promising interventions for more widespread implementation and to inform future research in this area. MEDLINE was searched up to September 2012, and relevant studies were identified using titles and abstracts. Full text articles were reviewed to make a final determination on inclusion. Relevant characteristics of the studies were extracted and summarized. Following a screening of 6,978 articles, 60 manuscripts were included. The majority of manuscripts were published during or after 2007. 63.3% of studies were pre-post comparisons, and 13.3% were randomized controlled trials. 56.7% of the studies were focused on pharmacotherapy. 71.7% of the studies resulted in statistically and clinically significant improvements in an explicit financial measure or a proxy financial measure. Only 15% of the studies directly measured the financial impact of an intervention, whereas the financial impact was inferred in the remainder of studies. Data on cost-effectiveness were available for only one study. Given these results, it is apparent that further research is needed on the cost impact and cost effectiveness of CDS in the inpatient setting.

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ACKNOWLEDGEMENTS

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BACKGROUND

Healthcare costs are increasing rapidly and at an unsustainable rate in many countries. In the United States, inpatient care is the single largest contributor to national health expenditures, accounting for 31.5% of $2.7 trillion dollars of health expenditures in 2011 [1]. As such, inpatient care is a significant driver of increased health spending. In 2011, the annual spending on hospital care in the U.S. grew 4.3% as compared to 3.9% growth in overall health expenditures [1]. Contributing to the importance of addressing inpatient costs is the fact that reducing these costs has the potential to financially benefit inpatient healthcare organizations regardless of reimbursement models. Traditional episode-of-care payment systems (for example, Medicare's inpatient prospective payment system), bundled payments systems, and comprehensive payment systems (embodied in accountable care organizations) are all examples of reimbursement models under which healthcare organizations stand to benefit from reducing inpatient costs [2].

Clinical decision support (CDS) represents a promising approach to both improving outcomes and decreasing costs [3]. Several past systematic reviews have examined outcomes related to clinical decision support systems in the inpatient setting, but few have focused on the impact of CDS on inpatient costs specifically [4-9]. One review published in 2006 evaluated cost as an outcome [10]. However, this review was focused on health information technology (IT) in general rather than CDS specifically. Moreover, it only included studies published through January 2004. A second, more

recent review on CDS included cost outcomes but was limited to studies with a randomized trial design [11]. The design and timing of these two reviews potentially excluded relevant CDS intervention trials. In particular, nonrandomized research designs are commonly used to evaluate CDS interventions.

Given the importance of limiting the growth of inpatient costs and the potential benefit of CDS, we sought to (i) inclusively identify promising interventions that could serve as models for more widespread implementation and to (ii) identify gaps in the literature warranting further research. As such, we systematically reviewed both randomized and nonrandomized trials of CDS systems with the potential to reduce inpatient or emergency department (ED) costs.

METHODS

Data source

Using a search strategy adapted from a previous systematic review [7], we searched MEDLINE through September 24, 2012. The latest search was performed on that date. We used a combination of the following search terms: *decision support systems, clinical; decision-making, computer-assisted; reminder systems; guideline adherence;* and *medical informatics*. Details of the search strategy are available in the Appendix. Search results were limited to human subjects and the English language.

Inclusion and Exclusion Criteria

We defined a CDS system as a system designed to directly aid in clinical decision making, in which characteristics of individual patients are matched to a knowledge base for the purpose of presenting patient-specific assessments or recommendations to clinicians [4]. Inclusion criteria were as follows: peer-reviewed primary manuscript; clinical trial of a CDS system in an inpatient or ED setting; and use of either cost or a proxy measure for cost (e.g., length of stay) as an outcome metric. Exclusion criteria were as follows: study not in English; or use of CDS in the control group.

Study Selection

Titles and abstracts from retrieved references were reviewed to determine potential inclusion eligibility. The full texts of studies that appeared to be potentially

eligible were then reviewed. Final inclusion determinations were made using the full texts. In cases where a study's inclusion status was unclear upon review by the primary reviewer, the authors jointly reviewed the study and made a consensus decision.

Data Extraction

For each article that met inclusion criteria, data were extracted on setting, trial design, intervention, and trial results. Abstracted trial results included outcomes with potential cost-saving implications, whether costs were directly measured, whether there was a statistically and clinically significant improvement in cost or in a proxy measure, and whether the study could be considered a cost-effectiveness study. Specifically, measures with potential cost-saving implications consisted of direct cost measures or other proxy measures with cost ramifications. Proxy cost measures included length of stay, adverse events, and process measures correlated with adverse events. Clinical significance of results was determined by author consensus. To be considered a cost effectiveness study, the study must have accounted at least for the personnel costs included in developing and deploying the intervention. For commercial CDS systems, at least the cost of licensing the software must also have been considered.

Data Analysis

Extracted data were analyzed and presented in table form and narrative summary. Additionally, significant themes, trends, and patterns were noted and discussed.

RESULTS AND DISCUSSION

The literature search returned a total of 6,978 unique references. 6,855 references were excluded after screening of titles and abstracts. We reviewed 123 full-text articles, of which 60 [12-71] met criteria for inclusion in the review (see Figure 1). Characteristics of these studies are summarized in Table 1.

Study Timing

A majority (55%) of studies were published during or after 2007 [39-71]. The earliest included study was published in 1989 [12]. This high concentration of studies published between 2007 and 2012 represents large recent growth in the evaluation of inpatient CDS systems and is consistent with increasing adoption of health IT generally.

Study Designs

Almost all (86.7%) [12-19, 21-23, 25-33, 35, 36, 38, 39, 41-43, 45-59, 61-63, 65-71] of the studies were quasi-experimental trials (i.e., studies that aim to evaluate interventions but that do not use randomization [72]). Overall, the most common design used in the studies was a pre-post comparison, wherein researchers used historical controls prior to the implementation of an intervention. Of the 60 studies, 40 (66.7%) were some form of pre-post comparison [12, 14-16, 18, 25-27, 29-33, 36, 38, 39, 41, 42,

46-59, 61-63, 66-68, 70, 71]. Only eight (13.3%) of the studies were randomized controlled trials [20, 24, 34, 37, 40, 44, 60, 64].

The frequent use of quasi-experimental designs in medical informatics evaluations has been noted previously [72, 73], and the results of this review are consistent. Given the overwhelming prevalence of quasi-experimental designs, reviews of CDS systems that only include RCTs are bound to exclude a large portion of the published literature. With respect to this systematic review, a deliberate decision was made to include quasi-experimental studies, as one of the primary goals of this study was to develop a comprehensive catalog of CDS interventions that have the potential for reducing inpatient costs. At the same time, the inclusion of quasi-experimental study designs may have resulted in the inclusion of studies that are more subject to bias than RCTs.

Study Quality

Given that the stated goals of this review are exploratory in nature, we opted not to perform a meta-analysis of the extracted data. Moreover, because we chose to be inclusive in study selection, the studies in the review were heterogeneous in terms of interventions, outcomes, and study design. Additionally, the actual number of studies that included explicit economic data was very small. These factors limit the extent to which a meaningful synthesis of data might be obtained from meta-analysis techniques.

However, under different circumstances if a meta-analysis were performed, it would be customary to evaluate the quality of the included studies to provide an indication as to the validity of aggregate conclusions. In a review where the study designs are primarily quasi-experimental (such as this review), certain factors make the

evaluation of quality difficult. One factor is the number of different types of trial designs that fall under the quasi-experimental category. Within the domain of medical informatics, one review identified eleven different quasi-experimental trial designs [72]. These designs fell under the following broad categories: (a) quasi-experimental designs without control groups, (b) quasi-experimental designs that use a control group but no pretest, (c) quasi-experimental designs that use control groups and pretests, and (d) interrupted time-series designs [72]. Presumably, different trial designs increase the difficulty of the evaluation process. Notably, the Cochrane Collaboration recommends that systematic reviews that include nonrandomized studies employ a dedicated methodologist to assist in the evaluation of bias within studies due to the difficulty of addressing multiple study designs [74].

A second factor potentially hindering this evaluation is the lack of widely accepted quality assessment tools for evaluation of nonrandomized intervention studies. One systematic review on this topic identified 194 tools that have been used to assess the quality of nonrandomized intervention studies [75]. However, the authors of this review concluded that only 6 of these tools were appropriate for use in systematic reviews and that most of these tools would benefit from further modification. If we were to perform a quality analysis in the current review, an appropriate tool might be the Quality Assessment Tool for Quantitative Studies [76]. This tool was initially developed for evaluation of studies in the public health domain where nonrandomized study designs are commonly used. The tool evaluates 6 primary components: selection bias, design, confounders, blinding, data collection methods, and withdrawals/dropouts [76]. The tool

is reportedly easy to use, is not time consuming, and has comprehensive documentation available to assist with use [75].

Clinical Focus

The most common clinical focus targeted by CDS systems in the review was pharmacotherapy, with 56.7% of studies focused on this area [12, 13, 15, 16, 19, 23, 25-27, 29-33, 35-38, 41, 42, 46, 47, 50, 51, 54, 55, 59, 62-66, 69, 71]. The second most common area of clinical focus was venous thromboembolism prophylaxis, which accounted for 11.7% of studies in the review [20, 21, 24, 34, 43, 44, 53]. Examples of other clinical areas addressed included blood transfusion management [39, 40, 57], sepsis management [56, 61], and heparin-induced thrombocytopenia diagnosis [49, 58].

The significant focus on pharmacotherapy within the included studies may reflect the importance of drug selection within computerized provider order entry (CPOE) systems, which are foundational to CDS in many inpatient settings. 51.7% [15, 16, 19, 21, 23, 24, 26, 27, 29-34, 36, 39-41, 47, 49, 50, 53, 54, 57, 59, 62, 65, 68-71] of the studies overall involved CDS in the context of CPOE, and 61.8% [15, 16, 19, 23, 26, 27, 29-33, 36, 41, 47, 50, 54, 59, 62, 65, 69, 71] of the pharmacotherapy studies involved CDS in this context.

Cost-Effectiveness

Only one of the 60 studies (1.7%) was considered to be a cost-effectiveness study [52]. This study evaluated the use of a well-known diagnostic decision support system, DXplain, with residents in a teaching hospital. The authors reported that access to DXplain had been provided at no charge for the purposes of the study, but that an annual

license would have cost their organization $4,000-$6,000 per year [52]. It is telling that the only study to address cost effectiveness in this review concerned a simple license to a stand-alone, diagnostic CDS system. The majority of the studies in this review dealt with more comprehensive, integrated systems either purchased through vendors or developed locally. Under those circumstances, providing information about cost of development, implementation, or licensing fees is presumably more difficult. However, the near complete lack of this type of information is concerning given the need for such cost-effectiveness information by public policy developers and decision makers within healthcare organizations.

Direct Measurement of Cost

Nine (15%) studies in the review directly measured costs [16, 23, 26, 27, 29, 37, 39, 42, 52]. Seven of these studies focused on pharmacotherapy [16, 23, 26, 27, 29, 37, 42], while the other two addressed management of blood transfusion [39] and general medical diagnosis [52]. These studies included one RCT [37], with the remainder of studies having a quasi-experimental design. Of these studies, four reported a statistically and clinically significant improvement in a cost measure [16, 37, 39, 52]. Except in one case as outlined, the cost involved in implementing these interventions was not studied. Because investments in CDS are like any other business investment, having only one side of the financial equation (cost impact) is insufficient for making public policy and business decisions.

Use of Proxy Cost Measures

85% of the studies in the review solely reported proxy measures as indicators of impact on cost [12-15, 17-22, 24, 25, 28, 30-36, 38, 40, 41, 43-51, 53-71]. The most commonly used type of proxy measure in this group was process measures that were associated with adverse events. Of the studies that solely used proxy measures, 60.8% reported this type of measure [13, 15, 17, 19, 21, 24, 25, 30, 32, 33, 35, 36, 41, 45-50, 54-56, 58-60, 62-64, 66, 68, 71]. Examples of other proxy measures reported by these studies included rates of adverse events (reported by 21.6% of studies [12, 15, 34, 43, 51, 53, 59, 65, 68, 69, 71]), length of stay (reported by 9.8% of studies [20, 44, 60, 61, 65]), and patient charges (reported by 5.9% of studies [14, 22, 28]).

As noted, a strikingly small percentage of the studies directly measured an intervention's impact on cost. Therefore, in the majority of cases, we were left to infer a possible cost savings from nonfinancial proxy measures. Doing so has some inherent limitations. For example, four studies reported patient charges as an outcome [14, 22, 28, 52]. This is not a direct measure of cost, and it can be unclear as to how charges actually relate to cost [77]. We assumed that an institution's costs were at least proportional to what it charged a patient. However, given that we did not know the actual relationship between costs and charges at any given institution, this assumption suffered from an element of uncertainty.

Other limitations of using proxy measures for cost were apparent in our data. Two studies reported no differences in actual measured costs but reported decreases in length of stay [23, 27]. For this review, we considered length of stay a reasonable proxy measure for cost. However, in these two instances, shorter lengths of stay did not coincide with

actual decreased costs. The reverse of this situation was present in two studies, where directly measured costs decreased, but no difference in length of stay was detected [37, 52]. It is notable that of the nine studies in the review that directly measured costs, four demonstrated discrepancies between explicit cost measures and available proxy cost measures.

Another limitation of using proxy measures is related to adverse events. We considered measures of adverse events an appropriate proxy measure for cost given the potential for these events to necessitate the utilization of additional resources. We went a step further and included process measures correlated with adverse events as proxy measures as well. For example, one study in the review reported the rate of compliance with venous thromboembolism prophylaxis guidelines (a process measure correlated with an adverse event) [21]. Alternatively, another study reported the actual incidence of venous thromboembolism (a measure of an adverse event) [34]. For this review, we made the assumption that an improvement in a process measure associated with an adverse event would be associated with an improvement in the incidence of that adverse event. Decreased incidence of an adverse event, in turn, would be associated with cost savings. However, in one study, process measures correlated with an adverse event were significantly improved, but there was no improvement in the incidence of the actual adverse event [59]. More perplexingly, another study reported improvements in a process measure, no improvement in the correlated adverse event, and a significant improvement in length of stay [65].

Improvement in Cost/Proxy Measures

43 (71.7%) of the studies reported a statistically and clinically significant improvement in a cost or proxy measure [12, 13, 15, 16, 18, 19, 21, 24, 28, 30-40, 43, 45-47, 51, 52, 54-60, 62-71]. However, when considered in the context of the lack of direct cost measurements, the limitations of proxy cost measures, and the prevalence of quasi-experimental designs, it is difficult to know what level of confidence to place in that finding. On the face of it, CDS does appear to be a promising intervention for reducing inpatient costs. However, further research is clearly needed in order to more concretely characterize the benefits that have been achieved and that might be achieved in the future.

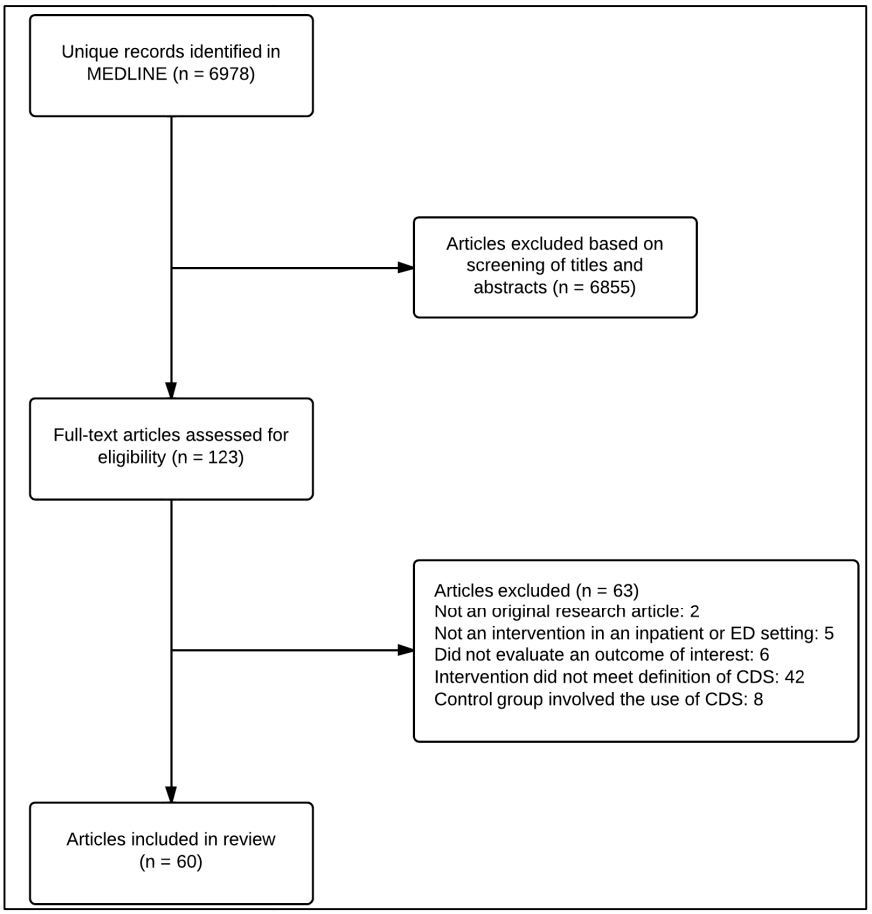

Figure 1, Study Selection Flow Chart

Table 1, Study Characteristics

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Larsen RA (1989) [12]	Teaching hospital	1 hospital; 6831 patients	Pre-post comparison	Computer generated paper reminders of need for perioperative antibiotics	Surgical wound infection rates	0.9% vs. 1.8% (P < 0.03)	No	Yes	Yes	No
Rind DM (1991)[13]	Teaching hospital	1 hospital; 10076 patients	Interrupted time series	CDS designed to alert physicians to rising creatinine levels in patients taking nephrotoxic drugs	Mean time from rise in creatinine to discontinuation or dose adjustment of nephrotoxic drug	72.6 vs. 93.7 hours (P < 0.001)	No	Yes	Yes	No
Day F (1995) [14]	Academic emergency department	1 emergency department; 465 patients	Pre-post comparison	Guideline-driven electronic charting system that provided recommendations for evaluation and treatment of patients with acute low back pain	Mean charges	$257 vs. $239 (NS)	No	No	No	No
Bates DW (1998) [15]	Academic hospital	1 hospital; 6711 admissions	Pre-post comparison	CPOE with CDS	Non-intercepted serious medication error rate	4.86 vs. 10.7 events/1000 patient days (P = 0.01)	No	Yes	Yes	No
					Preventable ADE rate	3.88 vs. 4.69 events/1000 patient days (NS)				
					Non-intercepted potential ADE rate	0.98 vs. 5.99 events/1000 patient days (P = 0.002)				

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Evans RS (1998) [16]	Teaching hospital	1 hospital; 1681 patients	Pre-post comparison	Comprehensive antimicrobial management system in an ICU setting	Mean total cost of hospitalization when computer regimen was followed	$26315 vs. $35283 (P < 0.001)	Yes	Yes	Yes	No
					Mean cost of antiinfective agents when computer regimen was followed	$102 vs. $340 (P < 0.001)				
					Total hospital length of stay when computer regimen was followed	10.0 vs. 12.9 days (P < 0.001)				
Knirsch CA (1998) [17]	Academic hospital	1 hospital; 43 patients	Prospective evaluation without control	Automated computer protocol for identification of patients requiring tuberculosis isolation combined with a clinical protocol	Isolation of culture positive tuberculosis patients within 24 hours of admission	79% vs. 70% (NS)	No	No	No	No
Aase O (1999)[18]	Academic emergency department	1 ED; 493 patients	Pre-post comparison	CDS using Bayes theorem to assist in diagnosis and triage of patients with acute chest pain	Percent of patients unnecessarily admitted to coronary care unit	19% vs. 35% (P < 0.05)[#]	No	No	Yes[#]	No

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Bates DW (1999) [19]	Academic hospital	1 Hospital; 1817 admissions	Time series: 1 baseline period, 3 intervention periods	CPOE + CDS with serial improvements of CDS across study periods	Non-missed-dose medication error rate	26.6 (final period) vs. 142 events/1000 patient days (P < 0.0001)	No	Yes	Yes	No
					Non-intercepted serious medication error rate	1.1 (final period) vs. 7.6 events/1000 patient days (P < 0.0003)				
East TD (1999) [20]	Academic and community hospitals	10 hospitals; 200 patients	RCT	CDS system for management of mechanical ventilation	ICU length of stay	27.6 vs. 25.2 days (NS)	No	NR	No	No
Durieux P (2000) [21]	Teaching hospital	1 hospital; 1971 patients	Interrupted time series	CDS system for provision of pharmacological VTE prophylaxis recommendations to orthopedic providers for post-operative patients	Rate of compliance with VTE prophylaxis guidelines	94.9% (95% CI: 92.5%-96.6%) vs. 82.8% (95% CI: 77.6%-87.1%)	No	Yes	Yes	No
Schriger DL (2000) [22]	Academic emergency department	1 hospital; 830 patients	Interrupted time series: off-on-off	Guideline-driven electronic charting system that provided recommendations for evaluation and treatment of febrile children less than 3 years old	Median charges	$216 (intervention) vs. $216 (baseline) vs. $222 (post-intervention) (NS)	No	No	No	No
					Mean charges	$387 (intervention) vs. $357 (baseline) vs. $635 (post-intervention) (NS)				

Table 1 Continued

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Chertow GM (2001) [23]	Teaching hospital	1 hospital; 17828 patients	Interrupted time series	CPOE with CDS that provided adjusted default dose and frequency for patients with renal insufficiency	Mean length of stay	4.3 vs. 4.5 days (P = 0.009)	Yes	Yes	No	No
					Mean total costs	$4881 vs. $4968 (NS)				
					Mean Pharmacy costs	$168 vs. $166 (NS)				
Dexter PR (2001) [24]	Teaching hospital	1 hospital; 6371 patients	RCT	Computer generated reminders of patient eligibility for preventive care measures including prophylactic heparin use in high risk patients	Rate of prophylactic heparin use in high risk patients	32.3% vs. 18.9% (P < 0.001)	No	Yes	Yes	No
Kellet J (2001)[25]	Community hospital	1 hospital; 894 patients	Pre-post comparison	CDS system designed to aid in the decision to treat cases of acute myocardial infarction with fibrinolytic therapy	Proportion of appropriate candidates who received fibrinolytic therapy	68.9% vs. 66.7% (NS)	No	No	No	No
Mullett CJ (2001) [26]	Teaching hospital	1 hospital; 1758 patients	Pre-post comparison	Comprehensive antimicrobial management system in a pediatric ICU setting	Mean hospital costs per patient	$28257 vs. $25032 (NS)	Yes	Yes	No	No
					Total antiinfectives cost	$289.60 vs. $274.79 (NS)				
					Total PICU antiinfectives cost	$183.53 vs. $177.03 (NS)				
					PICU length of stay	4.90 days vs. 4.93 days (NS)				
					Hospital length of stay	10.76 vs 10.76 days (NS)				

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Mekhjian HS (2002) [27]	Academic hospital system	2 hospitals; 28898 patients	Pre-post comparison	Comprehensive CPOE system with CDS for pharmacotherapy	Severity-adjusted total cost per admission at hospital #1	$5661 vs. $5697 (NS)	Yes	Yes	No	No
					Severity-adjusted total cost per admission at hospital #2	$6518 vs. $6427 (NS)				
					Severity-adjusted length of stay at hospital #1	3.71 vs. 3.91 days (P < 0.002)				
					Severity-adjusted length of stay at hospital #2	3.61 vs. 3.68 (NS)				
Buller-Close K (2003) [28]	Academic emergency department	1 hospital; 280 patients	Interrupted time series	Guideline-driven electronic charting system that provided recommendations for evaluation and treatment of occupational exposure to blood or body fluids	Median charges per patient	$392 (intervention) vs. $473 (baseline) (95% CI $51 to $161 difference in charges)	No	No	Yes	No
Fischer MA (2003) [29]	Academic hospital	1 hospital; 1045 orders in intervention phase	Pre-post comparison	CDS within CPOE system to identify and inform providers of patients who are eligible to transition from intravenous to oral route for five targeted medications	Change in IV defined daily dose	-11.1% (P = 0.002)	Yes	Yes	No	No
					Change in PO defined daily dose	+3.7% (P = 0.002)				
					Change in length of stay	+1.9% (P = N/A)				
					Change in total drug expenditures	+12% (P = N/A)				

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Galanter WL (2004) [30]	Academic hospital	1 hospital; 1596 alerting situations	Pre-post comparison	CDS designed to improve the safe use of digoxin by providing alerts related to digoxin, potassium, and magnesium serum levels	Unknown serum values checked within one hour	Improved with P < 0.01 for 3 of 3 measures	No	Yes	Yes	No
					Unknown serum values checked within 24 hours	Improved with P < 0.01 for 3 of 3 measures				
					Low serum values supplemented within one hour	Improved with P < 0.05 for 3 of 4 measures				
					Low serum values supplemented within 24 hours	Improved with P < .05 for 2 of 4 measures				
Hulgan T (2004) [31]	Academic hospital	1 hospital; 15194 orders	Pre-post comparison	CDS to promote the use of oral—versus IV—quinolones	Percent of quinolone orders for oral route	62.4% vs. 55.5% (P <= 0.001)	No	Yes	Yes	No
Potts AL (2004) [32]	Academic hospital	1 hospital; 514 patients	Pre-post comparison	CPOE with CDS in a pediatric ICU setting	Potential ADE rate	1.3 vs. 2.2 events per 100 orders (P <0.001)	No	Yes	Yes	No
					Medication prescribing error rate	0.2 vs. 30.1 events per 100 orders (P < 0.001)				
					Rule violation rate	0.1 vs. 6.8 events per 100 orders (P < 0.001)				

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Galanter WL (2005) [33]	Academic hospital	1 hospital; 410 alerts or alerting situations	Pre-post comparison	CDS system designed to alert providers attempting to order medication contraindicated for patients with renal insufficiency	Likelihood of patient receiving at least one dose of contraindicated medication	47% vs. 89% (p < 0.0001))	No	Yes	Yes	No
Kucher N (2005) [34]	Academic hospital	1 hospital; 2506 patients	RCT	CDS system to identify patients at risk for deep venous thrombosis and alert physicians	Rate of venous thromboembolism at 90 days Rate of pulmonary embolism at 90 days	4.9% vs. 8.2% (P = 0.001) 1.1% vs. 2.8% (P = 0.004)	No	Yes	Yes	No
Nash IS (2005) [35]	Academic hospital	1 hospital	Time series: 1 baseline period, 2 intervention periods	CDS to identify patients with renal impairment who had received excessive dosage of medication. Physicians were then notified by nursing staff in one intervention period and notified by pharmacists in the other intervention period	Rate of excessive dosing with nurse feedback Rate of excessive dosing with pharmacist feedback	17.3% vs. 23.2% (P < 0.05) 16.8% vs. 23.2% (P < 0.05)	No	Yes	Yes	No
Chan AL (2006) [36]	Community hospital	1 hospital	Pre-post comparison	CDS consisting of an automated gentamicin dosing calculator integrated into an ICU CPOE system	Frequency of undesirable serum gentamicin levels	13.5% vs. 32.7% (P < 0.05)*	No	Yes	Yes	No
McGregor JC (2006) [37]	Academic hospital	1 hospital	RCT	CDS to provide antimicrobial management support to the institution's antimicrobial management team	Average antimicrobial expenditures per patient Length of stay	$127.77 vs. $163.00 (P < 0.05)* 3.84 vs. 3.99 days (NS)	Yes	Yes	Yes	No

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Thursky KA (2006) [38]	Community hospital	1 hospital; 1060 admissions	Pre-post comparison	CDS for antibiotic management in an ICU setting	Odds patient prescribed carbapenems after adjusting for risk factors	OR = 0.61, 95% CI = 0.39-0.97	No	Yes	Yes	No
					Odds patient prescribed 3rd generation cephalosporin after adjusting for risk factors	OR = 0.58, 95% CI = 0.42-0.79				
					Odds patient prescribed vancomycin after adjusting for risk factors	OR = 0.67, 95% CI = 0.45-1.00				
Fernandez Perez ER (2007) [39]	Academic hospital	1 hospital; 2200 patients	Pre-post comparison	CDS for management of RBC transfusions in the ICU setting	RBC transfusion cost	$556226 vs. $616442 (P = N/A)	Yes	Yes	Yes	No
					Average number of units transfused per patient	1.3 vs. 1.5 units (P = 0.045)				
Rothschild JM (2007) [40]	Academic hospital	1 hospital; 1607 patients	RCT	CDS for management of blood product transfusions	Percent of transfusion orders which were not guideline compliant (typically unnecessary or excessive)	59.6% vs. 67.5% (P < 0.0001)	No	Yes	Yes	No
Vardi A (2007) [41]	Academic hospital	1 hospital; 60094 orders	Pre-post comparison	CDS designed to prevent medication errors for resuscitation drugs used in a pediatric critical care setting	Number of medication order errors	0 vs. 3 medication order errors (P = N/A)	No	No	No	No

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Buising KL (2008) [42]	Teaching hospital	1 hospital; 525 patients	Pre-post comparison	CDS designed to support adherence to community acquired pneumonia recommendations	Percent of antibiotic prescriptions concordant with recommendations	89.7% vs. 61.9% (P <0.01)	Yes	Yes	No	No
					Average cost of antibiotics per patient	$84.04 vs. $72.07 (P = N/A)				
Lecumberri R (2008) [43]	Academic hospital	1 hospital; 19338 patients	Time series: 1 baseline period, 2 intervention periods	CDS system for identification of patients at high risk for VTE and notification of physicians of the need for prophylaxis	VTE rate for 1st intervention period	1.74 vs. 3.26 events/1000 patients (P < 0.05)	No	Yes	Yes	No
					VTE rate for 2nd intervention period	1.67 vs. 3.26 events/1000 patients (P < 0.05)				
Roukema J (2008) [44]	Academic hospital	1 hospital; 164 patients	RCT	CDS system for the evaluation/management of children with fever without apparent cause in the ED setting	Median length of ED stay	138 vs. 123 minutes (NS)	No	No	No	No
					Frequency of lab orders	82% vs. 44% (P < 0.001)				
Eden A (2009) [45]	Community hospital	1 hospital; 995 patients	Time series: 1 baseline period, 2 intervention periods	CDS system designed to remind anesthesiologists to reactivate alarms following cardiopulmonary bypass	Rate of alarm reactivation for 1st intervention period	63% vs. 22% (P < 0.001)	No	Yes	Yes	No
					Rate of alarm reactivation for 2nd intervention period	83% vs. 22% (P < 0.001)				

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Flanders SJ (2009) [46]	Academic hospitals	2 hospitals; 1482582 glucose measures	Pre-post comparison	CDS system designed to prevent hyperglycemia in patients receiving IV insulin in the ICU setting	Odds of a glucose measure < 150 mg/dL during 1st year post-baseline	OR = 1.8, 95% CI = 1.78-1.82	No	No	Yes	No
					Odds of a glucose measure < 150 mg/dL during 2nd year post-baseline	OR = 2.16, 95% CI = 2.14-2.19				
					Odds of a glucose measure < 150 mg/dL during 3rd year post-baseline	OR = 2.28, 95% CI = 2.25-2.30				
Matsumura Y (2009) [47]	Academic hospital	1 hospital; 970 patients	Pre-post comparison	CDS implemented with CPOE to prevent the ordering of contraindicated medications for patients with renal insufficiency	Rate of discontinuation of contraindicated medication	54% vs. 24% (P = 0.01)	No	Yes	Yes	No
Niemi K (2009) [48]	Community hospital	1 hospital; 4090 patients	Pre-post comparison	CDS system for identification of patients with pneumonia or heart failure and recommendations to providers to meet quality indicators	Compliance with quality indicators for pneumonia and heart failure cases	One of six measures improved with statistical significance	No	Yes	No	No

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Riggio JM (2009) [49]	Academic hospital	1 hospital; 65604 admissions	Pre-post comparison	CDS system to assist in the early detection of HIT	Average time from fall in platelet count to heparin-induced thrombocytopenia testing	3.0 vs. 2.3 days (NS)	No	Yes	No	No
					Average time from fall in platelet count to heparin-induced thrombocytopenia therapy	15.0 vs. 19.3 days (NS)				
					Average time from fall in platelet count to discontinuation of heparin products	2.9 vs. 1.3 days (p = 0.04)				
Sellier E (2009) [50]	Teaching hospital	1 hospital; 603 patients	Pre-post comparison	CPOE with CDS intended to decrease the proportion of inappropriate prescriptions in patients with renal insufficiency	Proportion of inappropriate prescriptions	19.9% vs. 21.3% (NS)	No	Yes	No	No
Bertsche T (2010) [51]	Academic hospital	1 hospital; 265 patients	Pre-post comparison	CDS system designed to decrease the incidence of ADEs related to drug-drug interactions in patients prescribed >8 drugs in the ICU setting. Printed alerts were provided to physicians	Relative risk of patient experiencing at least one ADE due to drug-drug interactions	25% vs. 44% (P < 0.01)	No	No	Yes	No

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Elkin PL (2010) [52]	Academic hospital	1 hospital; 1737 cases	Pre-post comparison	Computer-based diagnostic decision support system made available to residents in a teaching hospital	Mean cost per diagnostically challenging case	$7382 vs. $8318 (P = 0.0054)	Yes	No	Yes	Yes
					Mean total charges per diagnostically challenging case	$11403 vs. $12684 (P = 0.0180)				
					Mean Medicare Part A charges per diagnostically challenging case	$9390 vs. $10422 (P = 0.0173)				
					Length of Stay	3.99 vs. 4.14 days (NS)				
Galanter WL (2010) [53]	Academic hospital	1 hospital; 38647 patients	Pre-post comparison	Mandatory VTE risk assessment form integrated into the hospital's CPOE system. System provided recommendations for pharmacological prophylaxis based on risk	Overall VTE rates	0.43% vs 0.51% (NS)	No	Yes	No	No
McCoy AB (2010) [54]	Academic hospital	1 hospital; 1659 patients	Pre-post comparison	CDS system integrated in CPOE system to improve medication ordering for patients with acute kidney injury	Rate of modification or discontinuation of contraindicated drugs	52.6 vs. 35.2 /100 events (P < 0.001)	No	Yes	Yes	No

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Roberts GW (2010) [55]	Teaching hospital	1 hospital; 1001 patients	Pre-post comparison	CDS system for recommendations on appropriate prescription of certain renally cleared drugs in patients with renal insufficiency	Enoxaparin dosing conformant with guideline	86% vs. 68% (P = 0.03)	No	Yes	Yes	No
					Gentamicin dosing conformant with guideline	87% vs. 63% (P = 0.01)				
					Vancomycin dosing conformant with guideline	77% vs. 47% (NS)				
					Rate of holding renally cleared drugs during periods of acute renal failure	62% vs. 38% (p = 0.01)				
Tafelski S (2010) [56]	Academic hospital	1 hospital; 186 patients	Pre-post comparison	CDS intended to assist in the management of sepsis and septic shock in an ICU setting	Concordance with sepsis management guidelines	90.8% vs. 39.8% (P < 0.05)	No	No	Yes	No
					Mean daily antibiotic usage	1.3 vs. 1.5 agents/day (P < 0.05)				
					Percent of ICU days which were antibiotic-free	25% vs. 18.4% (P < 0.05)				
Adams ES (2011) [57]	Academic hospital	1 hospital; 6785 discharges	Pre-post comparison	CDS system intended to support the management of children potentially needing RBC transfusions	Rate of RBC transfusions per patient	0.05 vs. 0.076 (P < 0.03)	No	Yes	Yes	No
					Estimated direct cost savings during intervention phase	$165000 (P = N/A)				

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Austrian JS (2011) [58]	Academic hospital	1 hospital; 2087 patients	Pre-post comparison	CDS system to assist in the early detection of HIT	Proportion of patients tested for HIT antibody within 24 hours of a qualifying drop in platelets	41.9% vs. 31.5% (P = 0.03)	No	Yes	Yes	No
					Proportion of patients for whom heparin was discontinued within 24 hours of a qualifying drop in platelets	26.5% vs. 21.2% (P = 0.01)				
					Proportion of patients above the median length of stay adjusted for comorbidities	50.3 vs. 49.7 (NS)				
Cox ZL (2011) [59]	Academic hospital	1 hospital; 216 patients	Pre-post comparison	CDS system to assist in the prescription of tobramycin and amikacin	Proportion of initial doses within 10% of the calculated recommended dose	80% vs. 40% (P < 0.001)	No	Yes	Yes	No
					Percentage of correct initial dosing interval	87% vs. 63% (P < 0.001)				
					Incidence of nephrotoxicity	17% vs. 25% (NS)				

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Fitzgerald M (2011) [60]	Teaching hospital	1 hospital; 1171 cases	RCT	CDS system to promote adherence to trauma protocols in the ED setting	Hospital length of stay	NS	No	No	Yes	No
					Average ICU length of stay	70 vs. 112 hours (NS)				
					Error rate per patient	2.13 vs. 2.30 errors per patient (P = 0.04)				
					Percent of patients who received packed red blood cells	66.1% vs. 84.9% (P < 0.001)				
Giuliano KK (2011) [61]	Community hospitals	2 hospitals; 135 patients	Pre-post comparison	CDS system designed to increase adherence to sepsis protocols in the ICU setting	Total hospital length of stay	17.8 vs. 15.7 days (NS)	No	No	No	No
					ICU length of stay	10.3 vs. 7.4 days (NS)				
Kazemi A (2011) [62]	Teaching hospital	1 hospital; 248 patients	Pre-post comparison	CDS implemented within a CPOE system in a neonatal ward setting. CDS was specifically designed to address medication dosing errors	Medication error rate	34% vs. 53% (P < 0.001)	No	Yes	Yes	No
Lipton JA (2011) [63]	Academic hospital	1 hospital; 667 patients	Pre-post comparison	CDS system intended to assist with the management of intravenous insulin therapy in a coronary critical care unit	Proportion of patients with a mean blood glucose level within the target range	43% vs. 31% (P = 0.01)	No	Yes	Yes	No
Mann EA (2011) [64]	Teaching hospital	1 hospital; 18 patients	Randomized crossover trial	CDS intended to support the management of insulin in burn patients in the ICU setting	Percent of time in target glucose range	47% vs. 41% (p < 0.05)	No	No	Yes	No

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Milani RV (2011) [65]	Academic hospital	1 hospital; 80 patients	Prospectively controlled trial	CPOE with CDS to assist the prescription of antithrombotics in patients with chronic kidney disease admitted for acute coronary syndrome	Proportion of patients who received contraindicated antithrombotics	0% vs 17% (P = 0.01)	No	Yes	Yes	No
					Proportion of patients who experienced in-hospital bleeding	9% vs. 21% (NS)				
					Length of stay	4.8 vs. 9.1 days (P = 0.01)				
Qian Q (2011) [66]	Academic hospital	1 hospital	Pre-post comparison	CDS system intended to alert physicians to patients with left ventricular systolic dysfunction who were not being treated with an ACEi/ARB agent	Percentage of ACEi/ARB adherence	97.6% vs. 88.4% (P < 0.01)	No	Yes	Yes	No
Salinas J (2011) [67]	Teaching hospital	1 hospital; 105 patients	Pre-post comparison	CDS system designed to support the fluid resuscitation of severely burned patients in the ICU setting	Mean ventilator free days	6.5 vs. 3.8 days (P < 0.05)	No	No	Yes	No
					Mean ICU free days	NS				

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Cho A (2012) [68]	Academic hospital	1 hospital; 463 patients	Pre-post comparison	CDS system intended to alert physicians to patients at high risk for contrast-induced AKI when ordering contrast-enhanced CT imaging	Percent of at-risk patients who received prophylaxis for contrast-induced AKI	55% vs. 25% (P < 0.001)	No	Yes	Yes	No
					Incidence of contrast-induced AKI among at-risk patients	3% vs. 10% (P < 0.02)				
Griffey RT (2012)[69]	Academic ED	1 ED; 1407 patients	Interrupted time-series	CDS system designed to guide medication dosing in geriatric patients in an ED setting	Proportion of orders consistent with dosing recommendations	31.4% vs. 23% (P < 0.001)	No	Yes	Yes	No
					Proportion of patients who experienced an ADE	3.4% vs. 7.1% (P = 0.02)				
					ED length of stay	5.6 vs. 5.8 hours (NS)				
Raja AS (2012) [70]	Academic ED	1 ED; 6838 patients	Pre-post comparison	CDS system intended to assist with the use of CT pulmonary angiography for acute pulmonary embolism	Quarterly utilization of CT pulmonary angiography	21.1 vs. 26.4 examinations/1000 patients (P = 0.0379)	No	No	Yes	No

Table 1 Continued

Citation	*Setting*	*Scope*	*Trial design*	*Intervention (control = usual care unless otherwise specified)*	*Measures with potential cost saving implications*	*Results (intervention vs. control)*	*Direct measurement of cost*	*Integrated with primary clinical information system*	*Statistically & clinically significant improvement in cost or proxy metric*	*Cost effectiveness study*
Wang H (2012) [71]	Teaching hospital	1 hospital; 38647 prescriptions	Pre-post comparison	CDS within CPOE system intended to prevent dosing errors of 13 antibiotics which require adjustment based on creatinine clearance	Percent of antibiotic prescriptions with an inappropriate dosage during the 4th year following implementation	3.42% vs. 21.3% (P < 0.001)	No	Yes	Yes	No
					Incidence rate of renal function deterioration during the 4th year following implementation	9.47% vs. 10.94 (P < 0.001)				

ACEi = angiotensin-converting-enzyme inhibitor; ADE = adverse drug event; AKI = acute kidney injury; ARB = angiotensin receptor blocker; CDS = clinical decision support; CPOE = computerized provider order entry; CT = computed tomography; ED = emergency department; HIT = heparin-induced thrombocytopenia; ICU = intensive care unit; NR = not reported; NS = not significant; OR = odds ratio; RBC = red blood cell; RCT = randomized controlled trial; VTE = venous thromboembolism

*P value not provided by manuscript; calculated using raw data provided in manuscript

#P value not provided by manuscript; calculated using raw data provided in manuscript; assumes historical control period had same sample size as intervention period

CONCLUSIONS

Health IT, and CDS in particular, has been touted for many years as a highly promising strategy for improving clinical care and "bending the cost curve" [78, 79]. However, more recent analyses have found that health IT systems such as EHR systems are not having the anticipated benefits in cost reduction [80, 81]. This study adds to these concerns that the potential benefits of health IT and CDS are not well grounded in empirical evidence, with only nine studies directly measuring costs and only one actually measuring cost-effectiveness of CDS for inpatient cost reduction.

As healthcare organizations continue to rapidly adopt health IT, leadership within those organizations must decide how to best use limited resources. Presumably, the potential cost savings associated with intervention candidates is a major factor in making those decisions. However, as a discipline, informatics does not appear to be meeting the needs of these healthcare decision makers with regard to CDS, as we have not been providing sufficient, rigorous data related to the cost benefits of CDS interventions in the inpatient setting. Further research with specific attention to cost implications of CDS systems is clearly needed.

APPENDIX

Detailed search strategy:

1. exp Decision Support Systems, Clinical/
2. Decision Making, Computer-Assisted/
3. exp Reminder Systems/
4. exp Guideline Adherence/
5. exp Medical Informatics/
6. 4 and 5
7. 1 or 2 or 3 or 6
8. limit 7 to (English language and humans)

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